LENA BCR-ABL1

BCR-ABL1 KINASE DOMAIN MUTATION SCREENING KIT

LENA – BCR ABL1
Kinase Domain Screening Test

BCR-ABL1 refers to a gene sequence found in an abnormal chromosome 22 of some people with certain forms of leukemia.

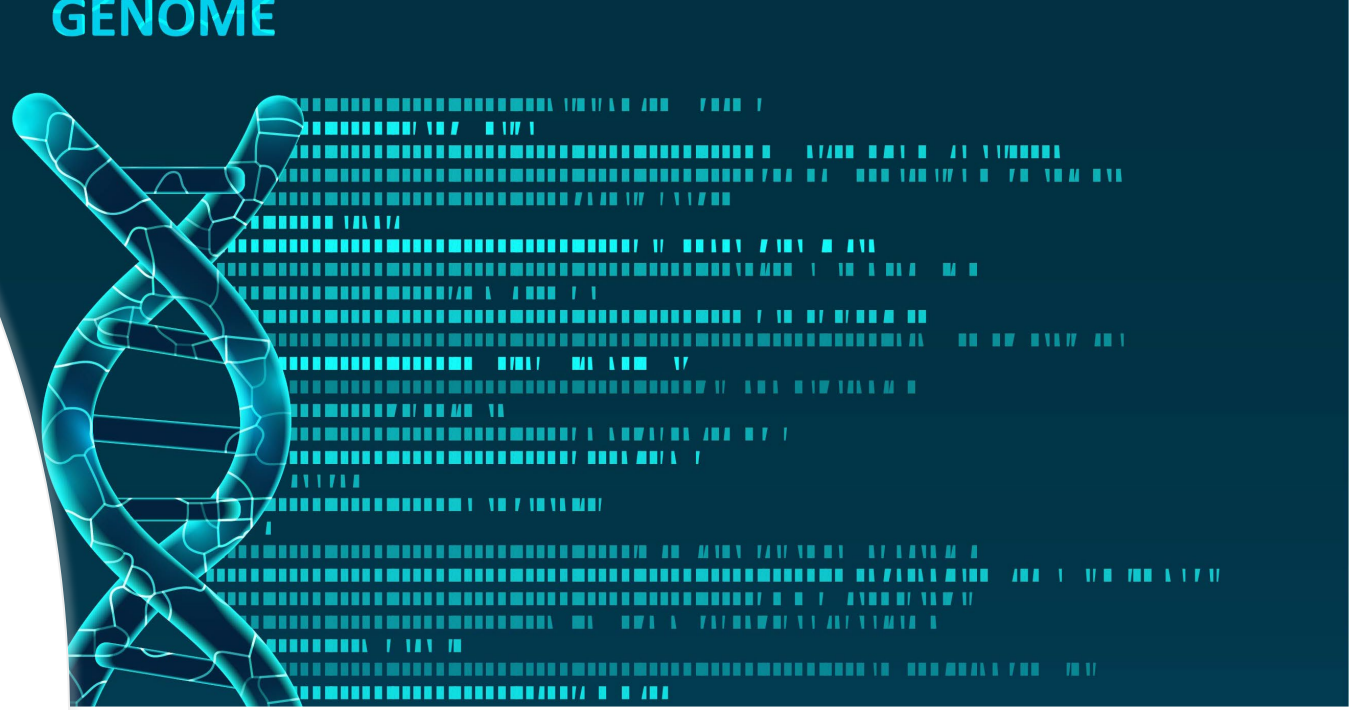
Unlike most cancers, the cause of chronic myelogenous leukemia (CML) and some other leukemias can be traced to a single, specific genetic abnormality in one chromosome.

The presence of the gene sequence known as *BCR-ABL1* confirms the diagnosis of CML and a form of acute lymphoblastic lymphoma (ALL), specifically a type of B-lymphoblastic leukemia/lymphoma.

In very rare cases, the abnormal chromosome is linked to cases of acute myeloid leukemia and T-lymphoblastic leukemia/lymphoma.

LENA BCR-ABL1
BCR-ABL1 KINASE DOMAIN MUTATION SCREENING KIT

LENA – BCR ABL1
Kinase Domain Screening Test



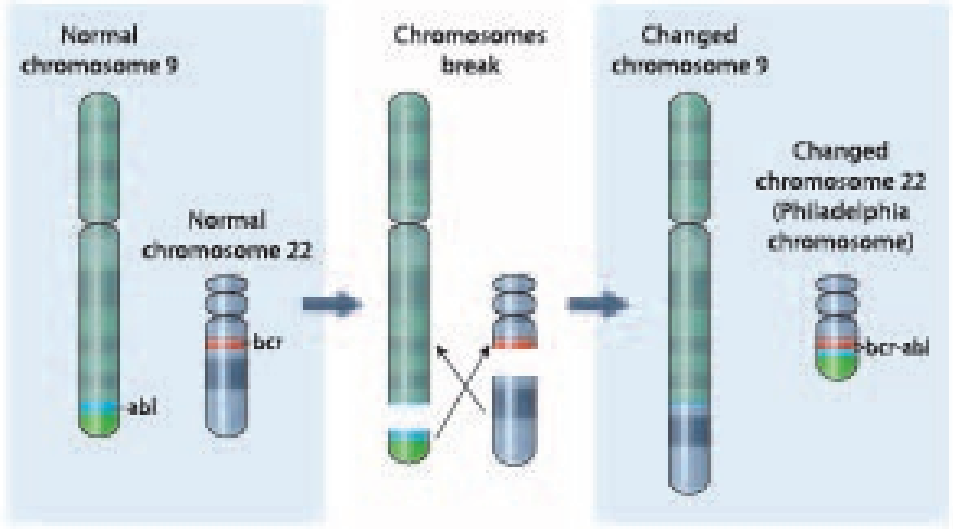
- Humans have 23 pairs of chromosomes containing inherited genetic information. Those genes contain the blueprints, in the form of DNA, for producing the proteins that our bodies rely on to function properly. While some genetic abnormalities are inherited, they can also come from changes that occur to genes or chromosomes after a person is born. This can happen through exposure to various environmental factors (e.g., radiation, certain chemicals) but more often for unknown reasons.

- The *BCR-ABL1* gene sequence is one such acquired change that is formed when pieces of chromosome 9 and chromosome 22 break off and switch places. When this occurs, the ABL1 region in chromosome 9 fuses with the BCR gene region in chromosome 22. This type of change is called a reciprocal translocation and is often abbreviated as t(9;22). The resulting chromosome 22 that has the *BCR-ABL1* gene sequence is known as the Philadelphia (Ph) chromosome because that is where it was first discovered.

LENA BCR-ABL1

BCR-ABL1 KINASE DOMAIN MUTATION SCREENING KIT

LENA – BCR ABL1
Kinase Domain Screening Test



- The resulting Philadelphia chromosome contains an abnormal *BCR-ABL1* fusion gene that encodes an abnormal protein that is responsible for the development of CML and a type of ALL. At diagnosis, 90-95% of cases of CML show a characteristic t(9;22) *BCR-ABL1* reciprocal chromosomal translocation. About 30% of adults with B-ALL have the translocation, while it is only present in about 2 to 4% of cases in children.

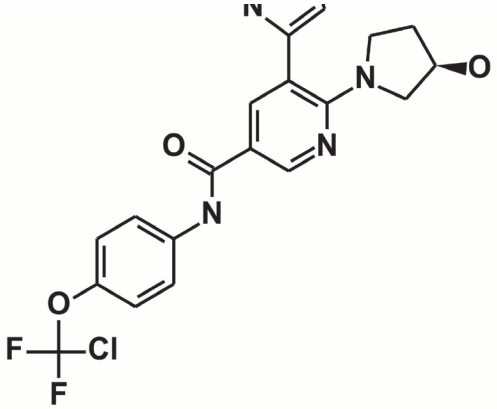
- The protein coded for by the abnormal *BCR-ABL1* fusion gene is a type of enzyme called a tyrosine kinase. That enzyme is responsible for the uncontrolled growth of leukemic cells. When large numbers of abnormal leukemic cells start to crowd out the normal blood cell precursors in the bone marrow, signs and symptoms of leukemia start to emerge. Treatment of these leukemias typically involves a tyrosine kinase inhibitor (TKI).

LENA BCR-ABL1

BCR-ABL1 KINASE DOMAIN MUTATION SCREENING KIT

LENA – BCR ABL1
Kinase Domain Screening Test

- Testing for *BCR-ABL1* detects the Philadelphia chromosome and *BCR-ABL1* fusion gene or its transcripts, which are the RNA copies made by the cell from the abnormal stretches of DNA. The presence of the *BCR-ABL1* abnormality confirms the clinical diagnosis of CML, a type of ALL, and rarely acute myeloid leukemia (AML).



Treatment for myeloid leukemia
(A kinase inhibitor)

LENA BCR-ABL1
BCR-ABL1 KINASE DOMAIN MUTATION SCREENING KIT

LENA – BCR ABL1 Kinase Domain Screening Test

LENA BCR-ABL1 kinase domain mutation detection adopts multi-color melting curve technology to monitor drug resistance in patients in time

1. 4-tube 4-color reaction system, easy to operate and easy to interpret
2. 40 mutation sites, covering more than 91% of ABL kinase mutations
3. The sensitivity is up to 5%, which is higher than Sanger sequencing and the detection result is reliable
4. The operation process same as qPCR, and the result can be obtained in 5.5 hours. Faster & cheaper vs. NGS

Covering More than 91% of ABL kinase mutation sites, enabling more accurate, easier and more convenient TKI resistance

Nr.	MUTATIONS SITES	Nr.	MUTATION SITES	Nr.	MUTATION SITES	Nr.	MUTATION SITES
1	p.M244V(c.730A ≥ G)	11	p.V3791 (c.1135G ≥A)	21	p.E225V (c.764A ≥T)	31	p.V299L (c.895G ≥T)
2	p.L248R (c.743T ≥G)	12	p.S417Y (c.1250C ≥A)	22	p.T315I (c.944C ≥T)	32	p.L248V (c.742C ≥G)
3	p.G250E (c.749G ≥A)	13	p.E459K (c.1375G ≥A)	23	p.F317L (c.951C ≥G)	33	p.252H (c.756G ≥C)
4	p.D276G (c.827A ≥G)	14	p.F486S (c.1457T ≥C)	24	p.F317L (c.951C ≥A)	34	p.252H (c.756G ≥T)
5	p.M351T (c.1052T ≥C)	15	p.Y253H (c.757T ≥C)	25	p.F317L (c.949T ≥C)	35	p.L298V (c.892CG)
6	p.E355G (c.1064A ≥G)	16	p.Y253F (c.758A ≥T)	26	p.F317V (c.949T ≥G)	36	p.F311I (c.931T ≥A)
7	p.L384M (c1150C ≥ A)	17	p.E255K (c.763G ≥A)	27	p.F317I (c.949T ≥A)	37	p.Y353H (c.1057T ≥C)
8	p.L387M (c.1159T ≥A)	18	p.F359C (c.1076T ≥G)	28	p.F317C (c.950T ≥G)	38	p.E355A (c.1046A ≥C)
9	p.H396R (c.1187A ≥G)	19	p.F359V (c.1075T ≥G)	29	p.T315A (c.943A ≥G)	39	p.E450G (c.1349A ≥G)
10	p.H396P (c.1187A ≥C)	20	p.F359I (c.1075T ≥A)	30	p.V299L (c.895G ≥C)	40	p.E459G (c.1376A ≥G)

LENA – BCR ABL1
Kinase Domain Screening Test

LENA BCR-ABL1 Kinase Domain Mutation Screening Kit

- dually labeled probes to target amplicons generated by PCR;
- then uses melting curve analysis to generate the minus derivative of the fluorescence intensity versus temperature, and
- compares the melting temperature (Tm) to gain mutation information of the sequences.
- LENA BCR-ABL1 is suitable for real-time PCR cyclers with FAM, HEX, ROX and Cy5 detection channels with melting curve analysis function.

LENA – BCR ABL1 Kinase Domain Screening Test

The kit can only detect 40 resistance mutations from exon 4 to exon 9 of ABL1 gene, other BCR-ABL1 kinase domain mutations are not covered.

BCR ABL1 Kinase region mutation detection effectively drug use

TKI DRUGS		MUTATION SITES
Resistance to First Generation druges	Imaninib	M0244V, L248R, V299L, G250E, Y253H, Y253F, E255K, E255V, D276G T315L, F317L, F317V, F317C, M351T, E355G, F359C, F359V, F359L L384M, L387M, V379L, H396R, H396P, S417Y, E459K, F486S
Resistance to second Generation Drugs	Nitotinib	Y253H, Y253F, E255K, E255V, F359C, F359V, F359I, T315I
	Dasatinib	V299L, T315A, F317L, F317V, F317I, F317C, T315I
	Bosutinib	E255K, T315I, V299L

LENA – BCR ABL1
Kinase Domain Screening Test

TEST PROCEDURE

1. Sample collection: Blood or bone marrow
2. Extraction of Total RNA
3. Reverse Transcription
4. Preamplification reaction
5. PCR and melting curve analysis.
6. Interpretation of the results

LENA – BCR ABL1 – Interpretation of results (I)

Detection Channel	Type of Mutation		Tm value
	Nucleic Acid Variation	Protein Variation	
A-FAM	C.1135G ≥ A	V3791	62.15=1.0C
	C.1076T≥G	F359C	70.20=1.0C
	c.944C≥T	T3151	82.39=1.0C
A-HEX			70.22=1.0C
A-ROX	c.730A≥G	M244V	57.40=1.0c
	c.1187A≥G	H396R	61.68=1.0C
	c.827A≥G	D276G	65.86=1.0C
	c.1052T≥C	M351T	70.01=1.0C
ACy5	c.749G≥A	G250E	64.78=1.0C
	c.1159T≥A	L387M	70.22=1.0C
	c.951C≥G	F317L	80.11=1.0C
B-FAM	c.1187A≥C	H396P	68.28=1.0C
	c.1150C≥A	L384M	82.29=1.0C
B-HEX			65.41=1.0C
B-ROX	c.892C≥G	L298V	57.18=1.0c
	c.1064A≥C	E355A	61.78=1.0c
	c.931T≥A	F311I	67.46=1.0c
	c.1064A≥G	E355G	71.70=1.0c
	c.756G≥C	Q252H	85.66=1.0c
B-Cy5	c.743T≥G	L248R	64.59=1.0c
	c.756G≥T	Q252H	69.12=1.0c
C-FAM	Cc.895G≥C	V299L	64.03=1.0c
	c.949T≥A	F317I	69.53=1.0c
	c.758A≥T	Y253F	77.91=1.0c
	c.1349A≥G	E450G	82.34=1.0c

LENA – BCR ABL1 – Interpretation of results (II)

C-HEX			68.04=1.0c
C.ROX	c.951C≥A	F317L	57.09=1.0c
	c.1375G≥A	E459K	67.56=1.0c
	c.949T≥C	F317L	71.60=1.0c
	c.1250T≥A	S417Y	86.03=1.0c
C-Cy5	c.757T≥C	Y253H	65.90=1.0c
	c.895G≥T	V299L	70.65=1.0c
	c.949T≥G	F317V	80.20=1.0c
D.FAM	c.950T≥G	F317C	62.01-1.0c
	c.1075T≥A	F359I	7.259=1.0c
	c.943A≥G	T315A	82.47=1.0c
D-HEX			67.73=1.0c
D-ROX	C.1075T≥G	F359V	56.84=1.0c
	c.1075T≥C	Y353H	61.47=1.0c
	c.1376A≥G	E459G	65.76=1.0c
	c.763G≥A	E255K	71.63=1.0c
D-Cy5	c.764A≥T	E255V	65.15=1.0c
	c.1457T≥C	F486S	70.67=1.0c
	c742C≥G	L248V	81.45=1.0c

LENA – BCR ABL1 Kinase Domain Screening Test

RECOMMENDED EQUIPMENT

Nucleic Acid Extraction System

LabAid 824S

qPCR Equipment SLAN 96S

info@alercell.com – Tel: (888) 960 0855